REMARKS

BASIS FOR AMENDMENTS OF CLAIMS

Claim 1 has been amended to clarify that the cell-surface gp120 and the number of lymphocytes in which are CD4 positive may be measured independently of each other. Support for this amendment is found throughout the specification, for example at page 6 line 21. Claim 4 has been amended to clarify that the measuring may be accomplished by FRET when the cell-surface gp120 and CD4 positive lymphocytes are measured. Claim 8 has been amended for grammatical reasons. Specifically the phrases "specific-for", "viral-infected" and "magnetically-separated" have been amended to remove these hyphens.

REJECTION UNDER SECTION 103

Claims 1-10 were rejected under 35 USC 103(a) as being unpatentable over U.S. Patent No. 5,597,688 of Connelly *et al.* (hereinafter Connelly) in view of U.S. Patent No. 5,817,458 of King *et al.* (hereinafter King). The Examiner argued that Connelly provided methods for the detection of HIV-1-infected cells employing a viral specific antibody (anti-p24) and a lymphocyte specific antibody (anti-CD4) to ascertain the infectivity status of any given patient. The Examiner admitted Connelly does not teach detection of gp120 on the surface of infected cells but argued that the combination of Connelly and King, which discloses detection of gp120 on the surface of infected cells would have made the present invention obvious. Applicants respectfully disagree with the Examiner's conclusion for the following reasons.

The Examiner has argued that it would have been obvious to have substituted the detection of cell surface gp120 as described in King for the internal marker p24 as described in Connelly. Applicants disagree with this conclusion for the following reasons. Connelly discloses at col. 30 line 56 the use of "antibodies to internal antigens such as HIV structural proteins". There is no suggestion in the Connelly reference to suggest use of cell surface antigens. The gp120 measured in the present invention is found on the cell surface of infected cells. Reichelderfer teaches in an article entitled "Laboratory Monitoring of the Viral Life Cycle" presented at 1998 Conference on the Laboratory Science of HIV that "2) increase our understanding that not all measurements will give the same results" at line 4 of the introduction on page 11 and further that "In the adage of the blind man and the elephant, each measurement offers a different perspective" in the Summary on page 16. The Reichelderfer reference suggests that different measurements of HIV infection provide different results. Therefore the ordinary artisan would not have an expectation of success that the gp120 marker disclosed in the King reference could be substituted for the p24 antigen in the Connelly reference to obtain a rapid and facile method for assessing the patient's infectivity status as suggested by the Examiner. In fact, the Reichelderfer reference would suggest that a different measure of HIV infection would provide different results and one cannot easily conclude that an internal antigen and a cell surface marker are interchangeable for assessing HIV infectivity status.

Further, the cells analyzed in the method of Connelly have been treated with a fixative (col. 4 lines 7-15) so that the cells are essentially "dead". In the present invention, no fixative is used and the cells to be analyzed are "live".

As presently claimed, cell surface gp120 and CD4 may be measured independently of each other. This has numerous advantages including increasing the flexibility of the assay. The limited disclosure of Connelly appears to describe at column 30 line 53 a mixture of antibody to CD4 and antibody to p24 so as to "determine not only how many CD4 positive cells the individual had, but also how many of the CD4 positive cells were expressing viral p24 antigen" (col. 30, lines 60-62). These methods of Connelly measure the two antigens in the same cell. There is no suggestion or teaching in the Connelly reference to measure two antigens independent of each other.

Finally some claims of the present invention claim the use of fluorescence resonance energy transfer assay, an assay that relies upon two antigens being in close proximity to produce a signal. The use of such an assay would be impossible with the antigens disclosed in the Connelly reference because one antigen is an internal marker and the other is a cell surface marker and therefore may not be sufficiently close to produce a detectable signal using fluorescence resonance energy transfer assay. There is not teaching or suggestion in the Connelly reference to use an antigen other than an internal antigen. Further there is no disclosure of fluorescence resonance energy transfer assay in the King reference. Therefore, the combination of Connelly and King fails to disclose the invention as presently claimed.

For all of the reasons mentioned above, Applicant's respectfully request the withdrawal of the rejection of Claims 1-10 as amended under 35 USC 103(a) as being unpatentable over Connelly in view of King.

REJECTION UNDER SECTION 112

Claims 11-16 were rejected under 35 USC 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. The Examiner argued that the disclosure fails to provide adequate guidance pertaining to the sensitivity of the claimed methodology. The Examiner argued that the patient has already tested negative by one virological assay (the coculture assay) ant the skilled artisan could reasonably assume that such patients are expressing minute quantities of antigen, if any so that an antibody-based assay, absent further sample manipulation, would not be expected to product the desired result. The Examiner concluded that the disclosure fails to provide any guidance or working embodiments to address this concern. Applicants respectfully disagree with the Examiner's conclusion for the following reasons.

A working example is not a requirement for an enabling disclosure (MPEP 2164.02). The disclosure of the present invention does suggest comparison with HIV culture to establish sensitivity, specificity, positive predictive value and accuracy (see Example page 8, lines 7-11 of the specification).

In the attached declaration, data is provided that in numerous instances of micrococulture negative samples, positive results were found using the Bio-Tech Imaging assay described in the instant application. The micrococulture data and immunoassay data described in the declaration were each conducted at independent laboratories between September 1999 and April 2000.

Thus the declaration shows, contrary to the Examiner's argument, that the present methodology for detecting gp120 on cell surface can be detected in patients negative by coculture in numerous instances.

CONCLUSION

Applicant respectfully requests that the Examiner consider these comments. Consideration and allowance of Claims 1-16 are respectfully requested. The Examiner is urged to contact Applicant to advance the prosecution of this application.

Respectfully submitted,

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Attachments:
Information Disclosure Statement and Reichelderfer reference
Declaration of Jennifer A. Grayson under 37 CFR 1.132